Orphan Drug Designation

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Designation Session Overview

- Purpose: Informative engaging informal
- 1st: Who is here and what are your needs?
 - Patients/industry/government
 - Beginner/intermediate/advanced knowledge
 - Basics/concepts/logistics/limitations/other
- 2nd: To the Powerpoint and points beyond....
- What next if you want more information and more engagement?

Orphan Drug Designation

Erica McNeilly Jeff Fritsch



The Value of Orphan Drug Designation

 The Orphan Drug Act established designation as a highly successful process

2,500+ products designated 390+ approved orphan drugs

Formal incentives

 Exclusivity
 Tax credits
 PDUFA fee exemption
 Grants

Informal incentive

Office of Orphan Products Development (OOPD) involvement Venture Capital

Orphan Drug Designation Application

Use the format found in 21 CFR 316.20(b)

or

Use the common EMA/FDA application

Answer all applicable questions Provide copies of all references

The Guts of the Application

- First/Foremost: What is the disease?
- Scientific Rationale Criteria: Is there "promise" that your drug will treat it?
- Prevalence Criteria: Is the disease rare?
- Clinical Superiority: Is your drug the same drug as one already approved for the same disease indication?

What is the disease?

- First question we ask...
- Sometimes this is straight forward; sometimes not.

- NO to salami slicing
- YES to "medically plausible subsets".

Medically Plausible Subset "Orphan Subset"

The drug would be expected to treat only a subset of disease and NOT the rest of the disease.

Example: A drug targets a protein found in only a rare subset of breast cancer cases ---YES.

Example: A drug to treat hypertension among left-handed people ---NO.

Example: A drug to treat kidney cancer among those failing 1st line treatment---NO.

Scientific Rationale Criteria

Must demonstrate that there is "promise" that the drug will be effective in treating said disease. "Promise" is interpreted to include—

- Data from clinical trials OR
- Data from case studies/reports OR
- Data from appropriate animal models OR (rarely)
- If no appropriate animal model data from in vitro experiments + support
- Note: these are data, not theories

Prevalence Criteria

- Consider all published estimates. Those on best epidemiologic grounds have preference.
- Extrapolate when necessary.
- Provide the prevalence estimate, not "<200,000".</p>
- When a range exists, we take the highest (unless justified otherwise).
- Expert opinions are a last-resort option.

Clinical Superiority

- Orphan-drug designation can be achieved for a same drug/indication as one that has marketing approval
- First, is the subsequent drug the same as the first drug?
- Definition in 21 CFR 316.3(b) (13)

 Small molecules with the same active moiety are the same drug

 Large molecules are same drug if principal molecular structural features are the same; however, this criterion is applied differently based on the kind of macromolecule. If subsequent drug is a same drug, the orphan drug designation application must provide a hypothesis for clinical superiority by a measure of:

- Greater effectiveness than the approved drug
- Greater safety in a substantial portion of the target population
- Or in unusual cases, demonstration of "a major contribution to patient care"

Generally, if the subsequent same product receives orphan drug designation based on clinical superiority, the superiority claim must be *demonstrated* in order to receive orphan drug exclusivity at the time of marketing approval.

When your application is ready to submit to OOPD...

Send 2 identical bound copies + signed cover letter (or one CDrom + signed cover letter) to:

Office of Orphan Products Development
Food and Drug Administration
W032-5271
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

What happens after submission?

- You will be sent a letter acknowledging receipt of the application.
- Reviewed by reviewer → designation Team Leader →OOPD director.
- Expect < 90 days to decision.</p>
- A negative decision can always be readdressed.
- Roughly 60-70% of applications result in granting orphan drug designation status.

Contacts and News

- Website <u>www.fda.gov/orphan</u>
 - Designation information and FAQ
- 301 796-8660 OOPD main line
 - jeff.fritsch@hhs.fda.gov 6-8682
 - debra.lewis@hhs.fda.gov 6-8661
 - e<u>rica.mcneilly@hhs.fda.gov</u> 6-8679
 - henry.startzman@hhs.fda.gov 6-8663
- Regulation Revision 21 CFR 316.20
- Workshop Fall 2012

